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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,277	03/06/2002	Thomas Ehrhardt	50716	2896

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,277	EHRHARDT ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,14,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,14,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. The Request for Continued Prosecution (RCE) under 37 CFR 1.114, filed 01.23.2006, based on parent Application No. 10/070,277 is acceptable and a RCE has been established. An action on the RCE follows.

2. Applicants' amendment filed with papers for RCE is also acknowledged.

3. Claims 9, 10, 14, 19 and 20 are pending and under consideration in this examination.

4. **Claims remain withdrawn** :

Claims 1-8, 11-13 & 15-18 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed as per response filed November 29, 2004.

5. Claims 9, 10, 14, 19 and 20 are under consideration in this examination.

6. Prior written description rejection is withdrawn since the amended claims recite both structure and function.

7. Claim Rejections - 35 USC § 112, first paragraph (Enablement)

Claims 9-10 & 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method (or process) for finding herbicidal active substances by inhibiting the activity of a plant dihydroorotase, comprising producing dihydroorotase recombinantly using the DNA sequence of SEQ ID NO: 1, does not reasonably provide enablement for using any DNA sequence having at least 60% homology to SEQ ID NO: 1 or 'using a DNA sequence of SEQ ID N: 1' which is interpreted here to mean a fragment of the DNA of SEQ ID NO: 1, and which encodes a protein having the enzymatic activity of a dihydroorotase. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 9-10 & 14 are so broad as to encompass a method of identifying an inhibitor of any dihydroorotase, which is encoded by a DNA having at least 60% identity to SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of dihydroorotase broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequence of SEQ ID NO: 1 and encoded amino acid sequence of dihydroorotase of SEQ ID NO : 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any dihydroorotase by modifying the DNA to

have a homology of at least 60% to SEQ ID NO: 1, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting dihydroorotase activity; (B) the general tolerance of dihydroorotase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any dihydroorotase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including dihydroorotase with an enormous number of amino acid modifications of the of SEQ ID NO: 2 [as a result of modifying the DNA]. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of dihydroorotase(s) having the desired biological characteristics, and further use in the method for identifying herbicidal compounds is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants' arguments (previous):

Applicants point out that in addition to SEQ ID NO: 1 from *S. tuberosum*, on page 2, line 9, DHO from *A. thaliana* is disclosed and this can be used according to the present invention. One of ordinary skill in the art easily would be able to find other DHO sequences, for example from other plant species based on sequence similarity or mutagenesis techniques. Also, functionally

unrelated DNA would not fall under the scope of present claim 9. Multienzyme DHO complexes such as those from yeast or *D. melanogaster* also would not be within the scope of claim 9 as they are not plants. DHO clearly is identified as an herbicide target.

Applicants also do not agree that the pending claims are directed to any DHO of certain homology, and the Applicants believe that screening for mutants DHO would be routine for one of ordinary skill in the art and can be done by *in vivo* mutagenesis. One of ordinary skill in the art would not have to undergo undue experimentation to obtain the modified DHO sequence[s]. Use of these sequences is illustrated in Greener et al. (1994).

In sum, Applicants respectfully request that the Examiner withdraw the rejection under 35 USC 112, paragraph, because the claims clearly recite both structure and function.

Applicants arguments have been considered and found to be persuasive, as far as the written description rejection is concerned, which rejection is hereby withdrawn.

However, Applicants arguments with respect to the enablement rejection is not found to be persuasive because Applicants have clearly failed to address the key issues of the rejection. In particular the specification does not support the broad scope of the claims which encompass all modifications of any dihydroorotase by modifying the DNA to have a homology of at least 60% to SEQ ID NO: 1, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting dihydroorotase activity; (B) the general tolerance of dihydroorotase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any dihydroorotase residues with an expectation of obtaining the desired biological

function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Also Applicants arguments that one of skill in the art can by *in vivo* mutagenesis to obtain modified sequences and with the aid of the works of Greener et al. use the sequences.

In response, Applicants do not explain how one of skill art will choose going about modifying the DNA sequences in order to encode a diverse range dihydroorotase, modified to the extent of 40%, which may be employed in the claimed method. Applicants present no details about the regions of dihydroorotase which can or cannot be modified because of the very nature of protein which may lead to an inactive protein. Thus leading to high unpredictability. Details of other non-enabling factors are explained in the enablement rejection.

The reference of Greener has limited use and does not teach applicability to any gene, is time consuming and expensive and only limited number of random mutants can be generated (*see* page 32, column 1-2), as against modifying a sequence (SEQ ID NO: 1) by 40%. Applicants' new arguments are a newer version of the old arguments and are considered no different to the previous arguments. The rejection is therefore maintained.

9. Claims 9-10 & 19-20 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: claim 9 - measuring the plant dihydroorotase in the presence and absence of a test substance, wherein the inhibition of dihydroorotase is indicative of screening a potential herbicidally active substance.

Claims 19 & 20 are included in this rejection for failing to correct the defect present in the base claim(s).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14, line 5, recites 'test substrate'. The claim is indefinite because the substrate for the enzymatic assay of the dihydroorotase is known. The 'test substance' is the unknown, which is being tested for it's inhibitory effect. Hence, replacing 'test substrate' with 'test substance' will overcome this rejection.

11. Addition of the following missing preposition is required in claim 14.
"DNA sequence **of** SEQ ID NO: 1.." , 'of' is missing.

12. No claim is allowed.

13. Method claims without the homology language will be in a better condition for allowance.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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